Remarks

Further and favorable reconsideration is respectfully requested in view of the foregoing amendments and following remarks.

Initially, although Applicants previously indicated, in responding to the requirement for restriction and election of species, that claims 1-11 and 15-18 read on the elected Western blot assay species (b)(i), the Examiner states that she has determined that claim 15, which refers to a bead-based assay and to "SELDI-TOF", does not read on this elected species.

However, claim 15 refers to SELDI-TOF **or conventional electrophoretical techniques**; and Applicants note that the Western blot assay, which is described on pages 7, 8 and 12 of the present specification, is a conventional electrophoretical technique. Accordingly, claim 15 should be examined along with claims 1-11 and 16-18.

The claims have been amended in response to the claim objections in items 5-8, by adopting the Examiner's suggested amendments, thus rendering these claim objections moot.

The claims have been further amended in response to the rejections under the second paragraph of 35 U.S.C. §112 in items 12-19 of the Office Action, thus rendering these rejections moot. Most of these amendments are self-explanatory. With regard to the amendment to the second step in claim 1, please refer to the disclosure at page 6, lines 8-9; page 9, lines 6-11; and Figs. 1-3. With regard to the amendment to claim 16, please see page 8, lines 19-21.

The rejection of claims 1-11 and 16-18 under the first paragraph of 35 U.S.C. §112 is respectfully traversed.

The Examiner is correct in stating that no working example is given wherein ocular autoantigens are detected in body fluids other than serum.

The present invention describes the use of autoantibodies in body fluids for the detection of glaucoma. Baldas et al. (Clinical Chemistry 2003) cited by the Examiner hypothesizes that anti-human transglutaminase antibodies are detectable in serum and saliva, but the use of saliva was not superior to sera in this particular study and disease. However, Applicants believe that these results cannot be generalized between **different**

diseases. What can be taken from this publication is the fact that indeed antibodies are found not only in serum but also in saliva.

It is known that there is a local production of antibodies in aqueous humor. The phenomenon that the amount of antibodies in aqueous humor is higher than in sera is called Goldmann and Wittmer coefficient. For example, N. Torun et al. (Ophthalmologe 99:109-112, 2002, text in German with English abstract, a copy of which is enclosed) could demonstrate that the analysis of aqueous humor is superior compared to serum analysis in the diagnosis of toxoplasmosis. A. Kijlstra et al. (International Ophthalmology 13:383-386, 1989, a copy of which is enclosed) compare antibody production in aqueous humor and serum as a diagnostic tool in toxoplasma uveitis. Anja Liekfeld et al. (Graefe's Arch Clin Exp Ophthalmol 238:222-227, 2000, a copy of which is enclosed) report on the analysis of aqueous humor and serum for the diagnosis of infectious uveitis. These publications demonstrate that aqueous humor is a source of antibodies comparable or even better than serum.

Antibodies found in tears may be used to diagnose dry-eye disease (F.H. Grus et al., Ophthalmologica 215:430-434, 2001, a copy of which is enclosed). This demonstrates that antibodies can be found in tears in addition to serum.

Taken together, these publications demonstrate that antibodies are available for diagnostic purposes in saliva, aqueous humor and tears in addition to serum, and it is known in the art that any of these body fluids may be used for diagnostic purposes. Applicants are therefore of the opinion that working examples for serum are sufficient support for the skilled person in the art, in order to enable him/her to apply the method of the invention also to other body fluid, since it is known that other body fluids display antibodies and therefore should be taken into consideration for diagnostic purposes.

Accordingly, Applicants take the position that, based on the art-recognized knowledge in this field, as shown by the publications referred to above, one of ordinary skill in the art would be able to practice the invention with other body fluids, in addition to serum.

For these reasons, Applicants respectfully submit that the rejection of the claims under the first paragraph of 35 U.S.C. §112 should be withdrawn.

The patentability of the presently claimed invention over the disclosures of the references relied upon by the Examiner in rejecting the claims will be apparent upon consideration of the following remarks.

Thus, the rejection of claims 1-6, 10-11 and 16-17 under 35 U.S.C. §102(b) as being anticipated by Joachim et al. is respectfully traversed.

This reference is an abstract which gives general hints, but no proper working conditions. Furthermore, the abstract only deals with detection of autoantibodies of retinal antigens and human subjects, digitations and analysis by multivariate statistical analysis. The abstract does not deal with a method of diagnosis of glaucoma. Amended claim 1 recites the particular step of comparing the pattern of autoantibodies of an individual with corresponding patterns of healthy individuals and glaucoma patients, and if the pattern of said individual is more related to the pattern of glaucoma patients than to the pattern of healthy individuals, glaucoma is diagnosed. This particular step is not mentioned in the abstract, and therefore the abstract neither anticipates nor suggests claim 1 and dependent claims 2-6, 10-11 and 16-17.

For these reasons, Applicants take the position that the claims are not anticipated by the Joachim et al. reference.

In response to item 23, Applicants confirm that the subject matter of the various claims was commonly owned by the joint inventors at the time the invention was made.

The rejection of claims 7-9 under 35 U.S.C. §103(a) as being unpatentable over Joachim et al. in view of Grus et al. is respectfully traversed.

The comments set forth above concerning the Joachim et al. reference are equally applicable to this rejection.

The Grus et al. reference relates to allopurinol-induced and methylprednisolone-induced changes in autoantibodies in rats suffering from uveitis. A method is presented which should allow an assessment of a treatment, because such a treatment influences the autoantibody composition. Although the statistical methods described in this publication may be related to the statistical method used in the present invention, it deals with uveitis and deals with the influence of a treatment of uveitis with allopurinol and methylprednisolone. Even combined with the abstract of Joachim et al., a method for diagnosis of glaucoma using autoantibodies and similar statistical methods (and in

particular claims 7-9) is not rendered obvious. The analysis in Grus et al. is not used for diagnostic purposes.

The rejection of claim 18 under 35 U.S.C. §103(a) as being unpatentable over Joachim et al. in view of Maruyama et al. is respectfully traversed.

The comments set forth above, concerning the Joachim et al. reference are equally applicable to this rejection.

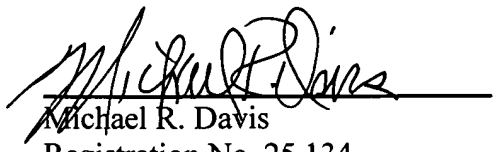
Maruyama et al. report on the relevance of Neuron Specific Enolase (NSE) in the pathogenesis of glaucoma. Autoantibodies against NSE are found only in 20% of glaucoma patients. For those patients showing NSE autoantibodies a decrease is observed with progression of the disease. It is immediately clear to the skilled person in the art that the determination of (single) autoantibodies against NSE in serum is not suitable for diagnosis of glaucoma. On page 131, right column, Maruyama et al. use contradictory wording for use in glaucoma diagnosis: How should NSE antibody titres be useful if it is only found in 20% of glaucoma patients, and furthermore when titres of anti-NSE antibody are almost the same among three different glaucoma stages (lines 9-11, right column page 131)? Since the skilled person in the art would not consider NSE autoantibodies as an indicator of glaucoma, combination of the knowledge from Maruyama et al. with the knowledge provided in the abstract of Joachim et al. would not make obvious the presently claimed diagnostic method using a change in the pattern of (several) autoantibodies to assess the progression and/or severity of glaucoma (claim 18) or the diagnostic method of claim 1 and the dependent claims.

For these reasons, Applicants take the position that the presently claimed invention is clearly patentable over the applied references.

Therefore, in view of the foregoing amendments and remarks, it is submitted that each of the grounds of objection and rejection set forth by the Examiner has been overcome, and that the application is in condition for allowance. Such allowance is solicited.

Respectfully submitted,

Franz GRUS et al.

By: 

Michael R. Davis
Registration No. 25,134
Attorney for Applicants

MRD/pth
Washington, D.C. 20006-1021
Telephone (202) 721-8200
Facsimile (202) 721-8250
August 30, 2006